Establishing payment models that support timely access to ATMPs

The purpose of this paper is to outline ABPI's recommendations for new payment models that could help manage two key challenges that are often associated with the reimbursement of ATMPs: affordability and uncertainty. While this paper has been developed with a focus on England, the discussion and recommendations are also useful for consideration across the devolved nations.

Executive summary

Advanced therapy medicinal products (ATMPs) are treatments with the potential to save, lengthen and improve patient lives by treating the root cause of diseases.[1-3] The UK Government has recognised the potential of ATMPs at the highest levels[4] and put in place several initiatives to help develop the UK as a world leader in the sector. Extensive work is underway across organisations, such as Genomics England UK[5], the Cell and Gene Therapy Catapult and the Accelerated Access Collaborative. The UK Government is working hard to create a regulatory, HTA and commercial environment through which suitable patients can access these transformative therapies.

However, a key challenge remains of how to reimburse these often single administration therapies which can have high upfront costs; and higher levels of uncertainty relating to longer-term outcomes. The key payment model related challenges for ATMPs can be characterised as affordability and uncertainty (magnitude and durability of clinical benefit). While it might be possible for health systems to absorb the upfront costs of these treatments when there are only a few new ATMP treatment launches per year and for small patient populations, affordability is likely to become a much more challenging and unavoidable issue, once the rich ATMP pipeline starts to deliver in increased numbers.[3] Over the next five years, approximately 20–30 new ATMP regulatory filings are expected annually in Europe[6] and the National Institute for Health and Care Excellence (NICE) expects to appraise around 30 ATMP topics by 2023.[7]

To date, NICE recommendations for ATMPs have been heavily reliant on simple discounts and Commercial Access Agreements, including flexibility for interim funding with further evidence collection supported by the Cancer Drugs Fund and in the future the Innovative Medicines Fund, are reliant on in-year funding.[8] This creates a challenge for funding ATMPs given their value is primarily (often) the potential for longer-term benefits. In several European markets, outcomes-based payments spread over multiple years have been established, breaking away from the existing restricted practice of the customary annual budget cycle of healthcare payers.[6] In France, the Economic Committee for Health products (CEPS) has

recently signed a 3-year pricing framework with the French Industry Association (LEEM) which recognises the need for measures to facilitate access to ATMPs, including 'split payments'.[9]

It is important that NICE and NHS England find a way to accommodate these transformative medicines at scale. From an HTA perspective there is an opportunity to evolve NICE's Technology Appraisal methods to be more suitable for evaluating ATMPs through the ongoing NICE Methods and Process Review, with some key proposals made around the discount rate, modifiers and how uncertainty is managed.[10]

From a reimbursement perspective, whilst the cancer drugs fund and innovative medicines fund can help address short term uncertainty challenges, these do not address longer-term uncertainty or affordability. Two key mechanisms that are likely to provide a more satisfactory solution for ATMPs are outcomes-based payments, and the option to spread treatment cost over a number of smaller payments over a fixed period.[11-13]

The ABPI welcomes the clarification provided in the NHS Commercial Framework for new medicines[14], but further NHS England engagement with industry is needed to address the unique challenges of ATMPs. Ideally, this should include further clarity on what would be deemed acceptable commercial models for ATMPs to facilitate more effective and efficient collaboration between industry and the NHS. Data collection requirements and accounting rules will need to be addressed to be able to consider outcome based and spread payment models that could help to address clinical uncertainty and manage budgetary impact.[15] Various examples of outcomes-based agreements for ATMPs from other European countries[6,16] alongside HM Treasury's preference for spread payments to be made over a period of seven years or less should be considered as an option for ATMP payment models in England.[17,18]

Alternative payment models that can help address the clinical uncertainties and affordability challenges facing ATMP should be proactively considered. Given the complexity of considerations for both payers and manufacturers, these will require a collaborative approach to assess acceptability, ensure feasibility and ultimately, secure access for patients.

Recommendations:

1. **NHS England, NICE and companies should engage early to assess, understand, and plan for potential future ATMP payment models required to enable patient access**. Clear touch points should be built throughout the process to clarify when to engage with NHS England and NICE.

2. **NHS England, DHSC, HM Treasury and other key financial stakeholders** should engage in discussions with industry to **identify any barriers to the introduction of innovative payment models**, such as split payments, and collaborate to consider what are the legislative, financial or structural barriers and how they can best be mitigated.

3. **NHS England** should in the first instance consider **additional support for two new types of innovative payment models** (outcomes-based payments and spread payments) through early dialogue with companies. The new Innovative Licensing and Access Pathway (ILAP) could also be utilised to help identify products that could be appropriate candidates for innovative payment models.

4. **NHS England** should **explore** with **NHS Digital and industry**, how best to collect data **for outcomes-based payment models**, and how ILAP could be an avenue to define requirements upfront to give time for data collection registries to be rolled out appropriately, especially if needs in England are different than in other geographies.

5. **NHS England and industry should** w**ork together through the Accelerated Access Collaborative (AAC) to test out the use of innovative payment models** for ATMPs **and take the learnings into relevant forums** to understand broader applicability and relevance for the system.

1. Introduction: ATMPs and the need for a holistic approach

Potential to transform

Advanced Therapy Medicinal Products (ATMPs) are recognised for their potential to revolutionise the way diseases are treated and to transform patient outcomes. Many of these products constitute a single treatment regimen offering life-long benefits to patients through potentially curative treatments, as well as offering significant savings to health services[3] by reducing or eliminating the need for complex chronic care regimes. ATMPs include cell, gene, tissue-engineered and somatic-cell therapy medicines.[2] They treat the root cause of diseases and disorders by augmenting, repairing, replacing, or regenerating organs, tissues, cells, genes and metabolic processes in the body.[1]

A diverse group of medicines

ATMPs do not form a homogenous group and include medicines to treat a wide range of severe, disabling or life-limiting[20] conditions for a variety of patient populations.[21] Just under half of ATMP pipeline products have narrowed their focus on rare diseases. [6]

Favourable UK environment

The UK Government has recognised the potential of ATMPs and put in place a number of initiatives to try to ensure that the UK can be a world leader in the sector through active support for research, product development and manufacturing:

- Innovate UK supports the Cell and Gene Therapy Catapult, which seeks to help organisations translate early research into commercially viable therapies[22]

- The Advanced Therapy Treatment Centre (ATTC) Network Programme operating within the NHS framework and coordinated by the Cell and Gene Therapy Catapult addresses the unique challenges of bringing ATMPs to patients

- The Accelerated Access Collaborative (AAC) has agreed coordinated plans to support the regulation, assessment and early adoption of ATMPs
- *Genome UK: the future of healthcare*, is a major policy initiative that sets out an ambition to create the most advanced genomics system in the world over the next ten years in the UK[5]
- More broadly, the Medicines Healthcare products Regulatory Agency (MHRA) has announced ILAP to reduce the time to market for innovative medicines[23], NICE is conducting a review of its methods and processes[10], NHS England has published a *Commercial Framework for new medicines*[14], the Department of Health and Social Care has published the *UK Rare Disease Framework* with a commitment within it to increase new treatment options[24], and the Innovative Medicines Fund (IMF) consultation is expected imminently.[25]

Significant challenges remain

However, the healthcare system continues to grapple with the challenges of how to reimburse ATMPs, specifically how to reimburse technologies that may be given as a one-time treatment, with a high upfront cost and potential uncertainty in long-term outcomes due to length of data available at time of HTA appraisal. This paper will reflect on the challenge in England specifically, what can be learned from other countries, and how the system may need to evolve in England.

Whilst only a handful[8] of ATMPs have received marketing authorisation to date, and even fewer treatments are currently reimbursed, the pipeline for ATMPs is strong.[6,26] it is already clear that countries without a robust, holistic approach to ATMPs, spanning clinical trials, through marketing authorisation, reimbursement and uptake, will be less attractive to companies as launch markets for their innovative products.

2. How can the UK be at the vanguard for ATMP commercial approaches?

ATMP opportunity for the UK

Now more than ever, the UK Government is keen to demonstrate its commitment to the life sciences sector by ensuring timely and equitable access to innovative medicines, including ATMPs. The desire to demonstrate leadership in relation to ATMPs is intensifying globally. With a broadly favourable policy environment for ATMPs, it is essential that the UK approach to payment models is aligned across all partners. This will ensure consistency of approach

from research to patient and deliver a coherent message that the UK welcomes these advanced innovative medicines.

Progress to date

The recently published NHS Commercial Framework for new medicines[14] emphasises the role that NHS commercial activity plays in ensuring patient access to the most clinically and cost-effective new treatments and technologies.

The document references how NHS England and NHS Improvement '*have already expanded the commercial flexibility offered to the industry*' and expresses an openness to '*complex confidential commercial arrangements*.' Indeed, there is detail on the broad range of schemes that would be acceptable and when.

Need for ATMP focused dialogue

The ABPI welcomes the clarity on commercial arrangements the NHS will consider but notes that there are challenges related to ATMPs which merit further engagement with industry. The eight[8,27] ATMPs that have been reimbursed in England to date rely heavily on existing payment mechanisms which may be unsustainable in the longer term.

There is concern that NHS England does not recognise or cannot accommodate the need for a new paradigm to ensure timely and equitable access to ATMPs, which challenge the constraints of annual budgeting.

As an example, Bluebird bio globally proposed a five-year, patient outcomes-driven instalment payment plan to balance affordability and share risk for its gene therapy Zynteglo across Europe. After the initial payment, the healthcare systems would only pay each year thereafter, if the patients continued to fully respond to the therapy.

3. The ATMP payment model challenge

Governments aim to ensure that patients in their country can access the most innovative treatments in a timely way, whilst maintaining health system sustainability through appropriate pricing agreements.

ATMPs present particular opportunities and challenges when it comes to payment models and can require a different approach to other medicines.[6] Whilst it is hard to generalise for such a diverse group of treatments, the key payment model related challenges for ATMPs can be characterised by affordability and uncertainty. Although these challenges can also apply to other types of medicines, it is recognised that the affordability and uncertainty challenges are significantly enhanced for ATMPs.

Affordability

ATMPs are delivering significant value to patients in terms of health outcomes, which can translate into a wider set of societal benefits. The price of ATMPs are linked to the added-value

that the medicine delivers. Some ATMPs can have a high upfront cost which, depending on the medicine in question, could be driven by a range of factors, including high manufacturing costs due to the personalised nature of the medicines and increased costs of clinical delivery, particularly where changes in infrastructure are required.[3] Nonetheless, ATMPs can offer a strong value proposition, and demonstrate significant incremental QALYs. The ABPI acknowledges the concerns some payers have around affordability; however the use of innovative payment models can help to mitigate this.

Unlike with many other medicines, these upfront costs would be expected to confer benefits to the patient over many years, if not a lifetime, without the need for additional treatment. In essence, the health system is being asked to pay for a treatment from its annual budget allocation, before the full value of that treatment has been realised by the patient, and society, and before the health service has been able to accrue any associated costs avoided in relation to care no longer needed by a particular patient.

It might be possible for health systems to absorb the upfront costs of these treatments when they are intended for a small patient population or when they are coming to market sporadically. However, the expectation is that some 20–30 new ATMP filings will be made in Europe annually over the next five years,[6] with NICE expecting to look at about 30 topics by 2023[7], which could present a greater challenge in terms of affordability, if there is a continued reliance on the annual budget cycle. Action is required to ensure patient access to innovative treatments is not delayed and spread payment models, that reimburse a company over a fixed number of years, can help address concerns with affordability and are a key part of the solution.

Uncertainty

ATMPs may be curative, life prolonging or life enhancing after a single treatment, which can create a degree of uncertainty for payers around the magnitude and durability of clinical benefit. Clinical trials will not extend to the length that the real-world benefit of a medicine is expected to endure. So, whilst trials will provide a degree of confidence in outcomes, they will not provide a guarantee. Furthermore, the full extent of the value delivered will not always be fully realised for many years. Concern that patients will undergo a loss of response over time can make it particularly hard to assess value and agree on an appropriate price for a product in a way that mitigates this risk for payers, despite there being no evidence to suggest the effects of ATMPs will reverse over time.

For companies, when health systems are unable to adequately assess and pay for the value delivered by ATMPs, this holds inherent risk that might detract from product development and clinical research in country or launch ambitions.

Health systems must find a way to recognise the value of these transformative medicines and alleviate the risk sitting with both payers and manufacturers. Payment models linked to patient outcomes will help to address this challenge.

4. Addressing commercial challenges for ATMPs

Payment models are a key lever in addressing both the affordability and uncertainty conundrums associated with ATMPs. Experts have been grappling with this challenge and a growing body of material has emerged to consider the role that payment models can play in ensuring timely and equitable access to ATMPs. Given the variety of ATMPs, although some may be suitable for reimbursement via existing options, others will require more flexibility to ensure the sizable pipeline is managed and delays to patient access are minimised.

Payment model options

Increasing numbers of ATMPs are making their way to market, suggesting that a viable business model may be starting to emerge. However, closer inspection of the payment approaches taken by different markets indicates there remains a reliance on traditional models in England. However, these models may not be sustainable once the ATMP pipeline starts to mature and provide the opportunity for patients to access an increasing number of these transformative treatments.

The two system challenges that the proposed commercial models will need to overcome are affordability and uncertainty. The two key mechanisms generally considered to provide solutions to these challenges are outcomes-based payment models, which link payment to outcomes achieved once the treatment has been administered, and spread payment models, which split the treatment cost over a number of smaller payments over a fixed period. In fact, most of the solutions proposed fall into one of these categories or a combination of the two.

Spreading payments over multiple years can help manage affordability and budget concerns. In England, short-term uncertainty can be managed with the CDF or forthcoming IMF. While long-term uncertainty can be partially managed by managed access agreements (MAAs) spread over several years, these or any other forms of commercial agreements cannot manage entire lifetime uncertainties. Therefore, decision-makers will also need to buy into the longer-term inherent risk associated with certain innovative treatments.

To date, there has been a heavy reliance on the use of the CDF and simple discounts delivered through Patient Access Schemes (PASs) and Commercial Access Agreements to bring ATMPs to market in England.[8] However, both of these approaches are reliant on the annual budget cycle, which is inappropriate for ATMPs over the longer-term for reasons discussed earlier in this paper.

Figure 1: Outcomes based payments overview[11-13]

Outcomes based payments	
How does it work?	• Outcomes-based payments are agreed on the basis of a product achieving certain outcomes, with reimbursement dependent upon the outcome criteria being met • Outcomes might be related to factors such as survival, return to normal activities, disease progression, relapse of recurrence or long term side effects • Real world data collection would need to ensure that evidence could be generated to demonstrate that agreed outcomes have been met over a period of time
Pros	• Overcomes common challenges whereby the data at launch does not provide sufficient confidence during reimbursement negotiations • Can increase payer and HTA body confidence in one-time treatments and reduce long-term uncertainties • Can balance the financial risk between payers and ATMP manufacturers • Fosters a consensus between patient demands for early access to innovative therapies and uncertainties on efficacy, safety and/or costs
Cons	• Payers and companies need to be aligned on evidential uncertainties, data gaps and the outcomes measured. Including any demonstration of cost savings • Healthcare professionals must 'buy-in' to the collection of quality data and agree to take on the administrative burden for data collection. Appropriate infrastructure must also be put in place • Failure to reach the specified clinical outcome could result in the manufacturer having to refund payments/forfeit subsequent payments

Figure 2: Spread payments overview[11-13]

Spread payments / annual payments / over time payments	
How does it work?	• Spreads the cost of an ATMP over a fixed period • May be linked to an outcomes-based approach to define criteria for payment release at agreed milestones • Appropriate for treatments where there is a short-term peak in patients waiting to be treated (high prevalence, low incidence) or budget expense
Pros	• High up-front costs spread across several years to facilitate appropriate resource allocation and affordable access • Reduces uncertainty around long-term performance and can ensure value for money
Cons	• Legislative and regulatory change changes may be required, including compliance of annual payments with public accounting rules • Administrative burden generally involved with this kind of contracts could discourage manufactures from entering negotiations • Need for both parties to agree on time period that is sufficient to assuage payer concerns about outcomes, affordability and financial risk but where manufacturer is able to accept terms from a commercial perspective • Overall cost could be higher for health service if manufacturer requires financing to bridge payment gap

Although outcomes are an important feature of interim arrangements like the CDF or the expected IMF, these approaches are also limited in that they place constructed parameters and predetermined budget pots around access. These limitations could lead to inequitable access to treatment, particularly for smaller, disadvantaged patient populations.

Hybrid manged entry agreements (MEAs) allow outcomes-based agreements and spread payments to be combined so that payments are made in instalments, and only if the treatment remains effective. Research into haemophilia gene therapies has suggested a novel approach in terms of 'reimbursement bands' with different reimbursement amounts associated with

different levels of patient response, after treatment has been administered[28] could be developed.

Learnings from other markets

By not offering innovative approaches, the UK is at risk of falling behind other markets in terms of access given several other European markets are already implementing outcomes based and spready payment models, whilst the US are exploring more novel payment approaches.

Spain and Italy have been particularly forward looking in their approach, implementing outcomes-based agreements to introduce ATMPs. In Spain, these agreements have been attached to payment cap agreements to address affordability and uncertainty for both payers and manufacturers. Italy has used MEAs, which have ensured faster ATMP assessments and patient access than other countries in the EU. These MEAs are essentially outcomes-based agreements and have been used for Strimvelis and Holoclar.[8] In both countries, deferred payments have been agreed, rather than be restricted by the customary annual budget cycle of healthcare payers and manufacturers.[6]

In Spain, Kymriah is reimbursed in the healthcare system through two outcomes-based, staged payments based on data collected through the Valtermed system; one payment at the time of treatment and the second at 18 months, provided the patient has achieved and sustained a complete response to the treatment.[16]

In Denmark, the Danish Medicines Agency reached a price agreement to fund Luxturna whereby regions pay for the drug in instalments and patients are required to check in at set times to monitor results. Subsequent instalments are only paid if the drug is effective.[29]

A three-year price-setting framework (2021-24) has been signed recently in France by the Comité économique des produits de santé (CEPS) and Les entreprises du médicament (LEEM). It recognises challenges for ATMPs and outlines measures to facilitate access to them. These include accountability measures such as risk-management contracts to consider uncertainty and guidance on discounts and splitting payments for innovative therapies.[9]

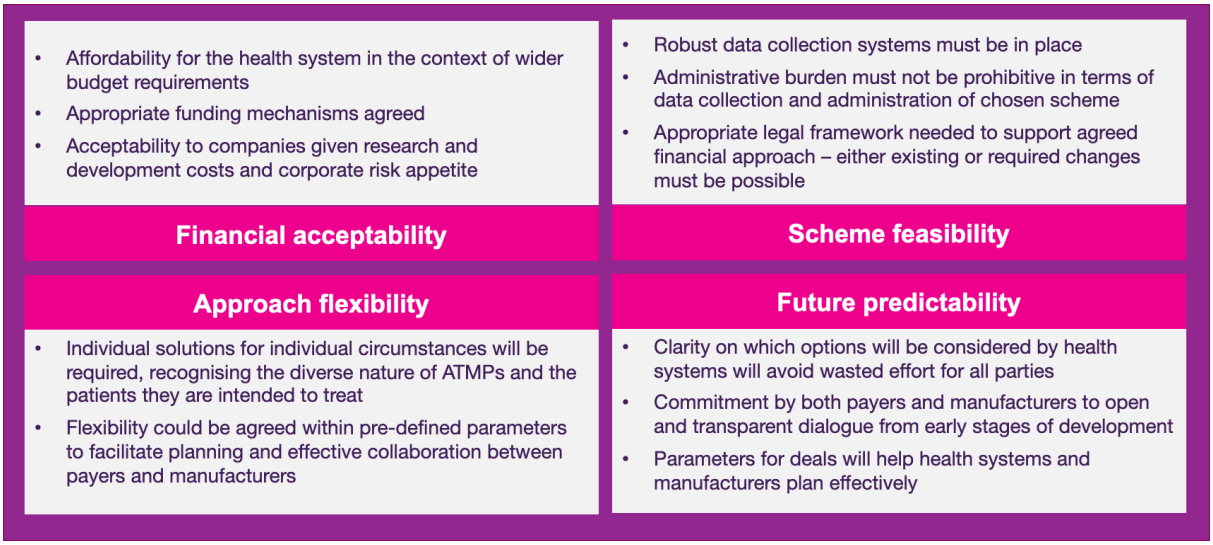
Further commercial models could also be considered as the environment evolves. For example in the US, Social Impact Bonds whereby a government specifies an outcome, and industry is reimbursed a set sum if the outcome is accomplished[30] are being considered. In situations where a company provides multiple treatment options for the same indication, lease models may also be considered, whereby the system moves towards procuring a treatment or outcome, rather than an individual product.[28]

Challenges to be addressed to facilitate innovative payment models in the UK

The introduction of innovative payment models to accommodate revolutionary treatments such as ATMPs requires a number of barriers to be overcome. These barriers include annual budgeting and the associated accounting constraints within the system, administrative burdens

of data collection and patient monitoring over time and engaging providers and commissioners with the challenges of ATMPs. Focusing on acceptability, feasibility, flexibility and predictability provides a helpful framework for managing uncertainties, as outlined below.

Figure 3: ATMP payment approach challenges



The importance of data collection

Potential hesitancy over the longer-term benefits of ATMPs can be reduced through the collection of real-world evidence and more innovative approaches to payment, such as outcomes-based solutions and other MAAs, will depend on it. As demonstrated in the recent response to the COVID pandemic, the NHS is in a unique position to collect, store and report on system wide data.

There is ongoing work in relation to data collection, such as that being led by the AAC, and we must continue to work together to set out the necessary core data requirements and work to implement these in routine care. We also need to consider how data can be collected and stored in a way that reduces administrative burden on those working on the frontline and ensures the collection of appropriate data to inform decision making over time.

There is a disparity of national registries for different diseases in England. There should be a levelling up to match the quality of registries such as the Systemic Anti-Cancer Therapy (SACT) chemotherapy dataset for cancer and the national registry for sickle cell disease. The proposed Medicines and Healthcare products Regulatory Agency (MHRA) national (UK wide) registries detailed in the Department of Health and Social Care white paper, *Working together to improve health and social care for all*,[19] and the data services of NHS Digital present opportunities to harmonise and simplify data collection and support the monitoring of ATMP treatment outcomes.

Budget management is vital

The NHS operates primarily on an annual budget cycle, which creates challenges in relation to spreading reimbursement over multiple years.

The Department of Health and Social Care is provided with an annual financial resource limit by HMT through which it subsequently allocates annual funds to the various national NHS arm's length bodies, including NHS England and NHS Improvement. Essentially these budgets are managed and accounted for on an annual basis, with limited ability to accrue future spend, and any overspends must be paid back in subsequent years, with significant associated sanctions which accompany them.[15]

Additionally within the system some organisations are issued with firm annual allocations for a period of two subsequent years, giving those organisations giving some level of short-term budget certainty. However, whilst this provides an element of short-term overall budget certainty, organisations are still required to account annually for their resources and therefore have limited ability to commit future financial resources with any certainty. Greater flexibility for the NHS to manage budgets and make firm commitments against future budgets across a number of years will be essential to facilitate spread payment models.

For companies, spread payments may also bring challenges relating to accountancy practices and risk associated with delayed payment for a product.

To develop a workable approach to spread payments, financial counterparts from the key policymaking bodies should engage with industry to see what might be possible and to identify which legislative, financial or structural barriers need to be removed or mitigated.

Recommendations:

1. **NHS England, NICE and companies should engage early to assess, understand, and plan for potential future ATMP payment models required to enable patient access**. Clear touch points should be built throughout the process to clarify when to engage with NHS England and NICE.
2. **NHS England, DHSC, HM Treasury and other key financial stakeholders** should engage in discussions with industry to **identify any barriers to the introduction of innovative payment models**, such as split payments, and collaborate to consider what are the legislative, financial or structural barriers and how they can best be mitigated.
3. **NHS England** should in the first instance consider **additional support for two new types of innovative payment models** (outcomes-based payments and spread payments) through early dialogue with companies. The new Innovative Licensing and Access Pathway (ILAP) could also be utilised to help identify products that could be appropriate candidates for innovative payment models.
4. **NHS England** should **explore** with **NHS Digital and industry**, how best to collect data **for outcomes-based payment models**, and how ILAP could be an avenue to define requirements upfront to give time for data collection registries to be rolled out appropriately, especially if needs in England are different than in other geographies.
5. **NHS England and industry should** w**ork together through the Accelerated Access Collaborative (AAC) to test out the use of innovative payment models** for ATMPs **and take the learnings into relevant forums** to understand broader applicability and relevance for the system.

References

1. Alliance for Regenerative Medicine, Fact sheet, accessed 9th March 2021. Available from: https://alliancerm.org/fact-sheet/.
2. European Medicines Agency: Advanced therapy medicinal products: Overview, accessed 9th March 2021. Available from: https://www.ema.europa.eu/en/human-regulatory/overview/advanced-therapy-medicinal-products-overview.
3. Marsden G, Towse A, Pearson S, Dreitlein B, Henshall C. *Gene therapy: understanding the science, assessing the evidence, and paying for value, March 2017.*
4. 10 Downing Street: Boris Johnson's first speech as Prime Minister: 24 July 2019, accessed 26th March 2021. Available from: https://www.gov.uk/government/speeches/boris-johnsons-first-speech-as-prime-minister-24-july-2019.
5. Gov.UK, Genome UK: the future of healthcare. Available from: https://www.gov.uk/government/publications/genome-uk-the-future-of-healthcare/genome-uk-the-future-of-healthcare.
6. Horgan D, Metspalu A, Ouillade M-C, et al. Propelling Healthcare with Advanced Therapy Medicinal Products: A Policy Discussion. *Biomedicine Hub.* 2020;5(3):1-23.
7. APM Health Europe: UK can do more on use of alternative payment models to support uptake of advanced therapies – NICE's Boysen, accessed April 2021.
8. Monocol Strategy & Communication: ATMP market entry from an HTA perspective, Region Skane, January 2020. Available from: https://atmpsweden.se/wp-content/uploads/2020/12/Bilaga-I-Rapport-ATMP_HTA-mapping-Europe-monocl.pdf.
9. LEEM: Régulation économique du médicament : Le Leem et le CEPS signent un nouvel accord-cadre pour trois ans (2021-2024), accessed March 2021. Available from: https://www.leem.org/presse/regulation-economique-du-medicament-le-leem-et-le-ceps-signent-un-nouvel-accord-cadre-pour.
10. NICE: Methods review consultation, December 2020. Available from: https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/chte-methods-consultation.
11. European Confederation of Pharmaceutical Entrepreneurs, ATMPs: New Payment and Funding Approaches, January 2021. Available from: https://www.eucope.org/paper-new-payment-funding-approaches-for-atmps/.
12. European Federation of Pharmaceutical Industries and Associations, Addressing Healthcare Challenges: Novel Pricing and Payment Models: New solutions to improve patient access, November 2019. Available from: https://efpia.eu/media/554543/novel-pricing-and-payment-models-new-solutions-to-improve-patient-access-300630.pdf.
13. Maes, I et al. Innovative funding solutions for paradigm changing advanced therapy medicinal products (ATMP) in Belgium, November 2019. Available from: https://www.inovigate.com/media/filer_public/e8/9c/e89ca2b0-1dcf-48fb-9afc-9e911ddcef84/innovative_funding_solutions_-_short_version_without_appendix_vs09.pdf.
14. NHS England: NHS commercial framework for new medicines, February 2021. Available from: https://www.england.nhs.uk/publication/nhs-commercial-framework-for-new-medicines/.
15. The King's Fund: Reforming the finances of the NHS, accessed 11th March 2021. Available from: https://www.kingsfund.org.uk/publications/reforming-finances-NHS.

16. Jørgensen J, Hanna E, Kefalas P. Outcomes-based reimbursement for gene therapies in practice: the experience of recently launched CAR-T cell therapies in major European countries. *Journal of market access & health policy.* 2020;8(1):1715536.
17. HM Treasury Managing Public Money, 2019. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/835558/Managing_Public_Money__MPM__with_annexes_2019.pdf.
18. National Audit Office: HM Treasury PF1 and PF2, January 2018. Available from: https://www.nao.org.uk/wp-content/uploads/2018/01/PFI-and-PF2.pdf.
19. DHSC: Integration and Innovation: working together to improve health and social care for all, accessed 17th March 2021. Available from: https://www.gov.uk/government/publications/working-together-to-improve-health-and-social-care-for-all.
20. European Confederation of Pharmaceutical Entrepreneurs, Gene and Cell Therapy – Pioneering Access for Groundbreaking Treatments, November 2018. Available from: https://www.eucope.org/wp-content/uploads/2019/03/eucope_genecell_therapy_november2018.pdf.
21. Rabbie, D. Taking Advanced Therapy Medicinal Products to Market, Cell and Gene Therapy Catapult, July 2018. Available from: https://ct.catapult.org.uk/sites/default/files/publication/DanRabbie_Taking%20Advanced%20Therapy%20Medicinal%20Products%20%28ATMPs%29%20to%20Market_29Jun18.pdf.
22. Cell and Gene Therapy Catapult, About Us, accessed 9th March 2021. Available from: https://ct.catapult.org.uk/about-us.
23. MHRA: The MHRA Innovative Licensing and Access Pathway is open for business, January 2021. https://www.gov.uk/government/news/the-mhra-innovative-licensing-and-access-pathway-is-open-for-business.
24. DHSC: UK Rare Disease Framework, January 2021. Available from: https://www.gov.uk/government/publications/uk-rare-diseases-framework.
25. UK Parliament: Medical Treatments, Question for Department of Health and Social Care, accessed April 2021. Available from: https://questions-statements.parliament.uk/written-questions/detail/2020-03-09/26941.
26. ABPI: Evolving the UK health system to support innovation for the rare disease community, Nicola Redfern, Feb 2021. Available from: https://www.abpi.org.uk/media-centre/blog/2021/february/evolving-the-uk-health-system-to-support-innovation-for-the-rare-disease-community/#9f0ea9e5.
27. NICE: NICE approves life-changing gene therapy for treating spinal muscular atrophy, accessed 11th March 2021. Available from: https://www.nice.org.uk/news/article/nice-approves-life-changing-gene-therapy-for-treating-spinal-muscular-atrophy.
28. Noone D, Coffin D, Pierce GF. Reimbursing the value of gene therapy care in an era of uncertainty. *Haemophilia.* 2021;27(1):12-18.
29. Medicinrådet: Medicinrådet anbefaler Luxturna som standardbehandling, accessed March 2021. Available from: https://medicinraadet.dk/nyheder/2020/medicinradet-anbefaler-luxturna-som-standardbehandling.
30. Findacure, Drug Repositioning and social impact bonds, accessed April 2021. Available from: https://www.findacure.org.uk/2015/01/09/drug-repositioning-and-social-impact-bonds/.